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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,100	01/16/2001	Rebecca E. Cahoon	BB-1174	3051

23906 7590 10/21/2003

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	27

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/744,100	CAHOON ET AL.	
	Examin r	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *6 and 8-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,9 and 11* is/are rejected.

7)☒ Claim(s) *8 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants amendment of the specification, cancellation of claims 1-5 and 7, amendment of claims 6, and the addition of new claims 8-11, Paper No. 21, 8/4/2003, is acknowledged. Claims 6 and 8-11 are still at issue and are present for examination.

Election/Restrictions

Applicant's election without traverse of Group III, Claims 6 and 8-11 in Paper No. 21 is acknowledged. As claim 6 and newly added claims 8-11 have been previously grouped with Group II, drawn to polynucleotides, applicants representative was contacted by telephone on 10/8/2003, at which point Lori Beardell confirmed this mistake and that applicants meant to elect Group **II**, claims 6 and 8-11.

Priority

Applicants statements that this application claims the benefit of U.S. Provisional application 60/093,209, filed July 17 1998, is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosures, Paper No. 7, filed 5/29/2001, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

Applicants description of Figure 1A-B references each of the Sequence identifiers listed in the figure with the exception of SEQ ID NO: 8. It is suggested that applicants maintain consistency and include a reference to this sequence identifier also in the description of the figure.

Appropriate correction is required.

Claim Objections

Claims 8-11 are objected to because of the following informalities:

Claims 8 recites "position 19-is", "position 22-is" and "position 184-is". The hyphen after 19, 22 and 184 should be removed to maintain consistency with the other designated positions of the claimed protein. Similarly claims 9 (position 19 and 184) 10 (position 19 and 184) and 11 (position 19 and 184) should be similarly amended.

Claims 8, 10 and 11 depend from rejected claim 6.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite in that it is confusing in its recitation "the sequence set forth in SEQ ID NO: 12, where: Axe at position 2 is Leu or Met, ...and Axe at position 317 is His or Ile." This recitation of each of the variable positions of SEQ ID NO: 12 is confusing because SEQ ID NO: 12 as defined in the sequence listing includes all of these variable positions and the different amino acid residues substituted at each position, thus the inclusion of this information additionally in the claim is confusing.

Claim 6 recites the limitation "wherein the polypeptide" referring to the encoded N-acetylglutamate kinase. It is suggested that for clarity sake, this be amended to "wherein the N-acetylglutamate kinase ".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 9 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly added limitation of claim 6 which recites "based on the Clustal V method" is not supported by the original specification. While page 5, lines 28-34 discuss "Multiple alignment of the sequences was performed using the Clustal method of alignment...", there is no support for the "Clustal V method of alignment".

Newly added claims 9 and 11 which are drawn to specific polynucleotide species of the genus of polynucleotides claimed in claim 6, are not supported by the original specification. Applicants attention is drawn to the specific limitations at position 198 for claim 9 and positions139, 152, 153, 156, 158 and 163 for claim 11.

Claims 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide comprising a nucleotide sequence encoding a N-acetylglutamate kinase wherein the N-acetylglutamate kinase polypeptide ha the amino acid sequence of SEQ ID NO: 12, does not reasonably provide enablement for any isolated polynucleotide comprising a nucleotide sequence encoding a N-acetylglutamate kinase wherein the N-acetylglutamate kinase polypeptide has an amino acid sequence of at least 95% sequence identity when compared to the sequence set forth in SEQ ID NO: 12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir.

1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 6 is so broad as to encompass any isolated polynucleotide comprising a nucleotide sequence encoding a N-acetylglutamate kinase wherein the N-acetylglutamate kinase polypeptide has an amino acid sequence of at least 95% sequence identity when compared to the sequence set forth in SEQ ID NO: 12. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, are drawn to a large genus of polynucleotides of which a in sufficient number of species are disclosed. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those polynucleotides which encode SEQ ID NOs: 2, 4, 6 and 8.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass the claimed modifications and fragments of a polynucleotide having at least 95% sequence identity to SEQ ID NO: 12, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting N-acetylglutamate kinase activity; (B) the general tolerance of N-acetylglutamate kinases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a N-acetylglutamate kinase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the N-acetylglutamate kinase activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary

Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides encoding a N-acetylglutamate kinase, wherein said N-acetylglutamate kinase comprises an amino acid sequence of at least 95% sequence identity to SEQ ID NO: 12.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including an isolated polynucleotide comprising a nucleotide sequence encoding a N-acetylglutamate kinase, wherein the N-acetylglutamate kinase has an amino acid sequence of at least 95% sequence identity to SEQ ID NO: 12. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax

phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
10/9/2003